II. REMARKS

Before the amendments made herein claims 71 to 80 were pending. Claims 71, 72 and 75-78 have been canceled herein without prejudice, and claims 81 to 89 added. Accordingly, after the amendments made herein are entered, claims 73, 74 and 79 to 89 will be pending.

A. Regarding the amendments.

Claims 73 and 79 have been amended to correct typos (misplaced commas).

New claims 81 and 86 are directed to the inactive pro-enzyme form. Support for these claims can be found in the specification, for example, at page 32, lines 1-3.

New claims 82 to 84 are directed to specific cells that are disclosed in the specification, for example, at page 30, lines 22-23.

New claims 85 and 87 are directed to tissues that are disclosed in the specification, for example, at page 34, lines 13-18.

Finally, new claims 88 and 89 track claims 73 and 74, respectively. Support for these claims can be found in the specification, for example, at page 30, line 17, to page 31, line 4.

Because the amended and new claims are fully supported by the specification, no issue of new matter arises.

B. Regarding the written description rejection.

Claims 71 to 78 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicant respectfully traverses the rejection.

The Action takes the position that the recited phrase "none of said somatic mammalian cells in said preparation is genetically modified to express heparanase" is not supported by the written description of the specification. The Action argues that there are situations where one

would genetically modify cells to express heparanase but not secrete it. Applicant respectfully disagrees. If one were to add heparanase to cells, there is no logical reason to genetically modify the cells to express heparanase for either expression or secretion purposes. Nevertheless, to promote the prosecution of this case, Applicant has canceled the claims that recite this phrase, so the issue is moot.

The Action again takes the position that the recited phrases "ex vivo," "somatic" and "mammalian" are not supported by the written description of the specification. While Applicant continues to disagree with this position for the reasons stated in previous responses, to promote the prosecution of this case, Applicant has canceled the claims that recite these phrases, so the issue is also moot.

Applicants note that claims 73 and 74 continue to be rejected as failing to comply with the written description requirement. However, these claims, as amended in the previous response, no longer recite any of the phrases objected to by the Action. Accordingly, Applicant respectfully requests that this rejection be withdrawn with respect to claims 73 and 74.

C. Regarding anticipation

Claims 71, 72, 73, 74, 76 and 79 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by U.S. Patent No. 5,968,822 (the '822 patent). Applicant respectfully traverses the rejection, noting that claims 71, 72 and 76 have been canceled herein without prejudice.

To maintain its anticipation rejection, the Action argues that "an inherent property of the insect cultures expressing . . . heparanase . . . is that the excreted heparanase would externally adhere to said cells." However, this is not inherent. Cells require heparan sulfate on their surface in order for heparanase to externally adhere to them. CHO 745 cells, for example, have not shown external adherence for this reason. In the case of High Five cells or Sf21 cells taught in the '822 patent, there is no evidence of external adherence. Therefore, there can be no basis for alleging inherency. See Declaration of Iris Pecker, paragraph 2.

Furthermore, claims 73, 74 and 79 require that heparanase be added to a cell preparation, while the '822 patent does not teach or suggest this feature. Such a feature can be distinguished by those skilled in the art. See Declaration of Iris Pecker, paragraph 3.

For example, when the pro-enzyme form of heparanase (P60) is added to cells, as required by claims 81 and 86, it can be detected in the cells by Western blot. However, P60 is not detected in cells that express heparanase (either naturally expressed or expressed through genetic modification), including the High Five and Sf21 cells taught in the '822 patent. See Declaration of Iris Pecker, paragraph 4.

In summary, there is no basis for alleging that it is inherent that secreted heparanase would adhere to cells. Moreover, the skilled artisan can distinguish between cells modified to secret heparanase and cells where heparanase is added. For these reasons, Applicant respectfully requests that this rejection be withdrawn.

D. Regarding obviousness

Claims 73, 74, 76, 77, 79 and 80 are rejected under 35 U.S.C. § 103(a) as allegedly obvious in view of the '822 patent and U.S. Patent No. 5,360,735 (the '735 patent). Applicant respectfully traverses the rejection, noting that claims 76 and 77 have been canceled herein without prejudice.

First, the Action argues that secreted heparanase would inherently externally adhere to cells. However, as discussed above, there is no basis for this allegation.

Second, the Action argues that it would have been obvious to express the mammalian heparanase taught in the '822 patent in the (mammalian) fibroblasts of the '735 patent so that the produced protein would be subject to proper post-translational processing.

In response, Applicant notes that claims 73, 74 and 79 each require that heparanase be added to the cells. In contrast, neither the '822 patent nor the '735 patent (or the combination of the two) teach or suggest this feature.

Moreover, Applicant respectfully submits that expressing mammalian heparanase taught by the '822 patent in the mammalian cell line taught by the '735 patent, so as to have "cells in suspension and a purified mammalian heparanase enzyme being externally adhered to said cells, thereby increasing the natural amount of heparanase externally adhered to said cells," as required by the claims, at the time of the subject invention, was at best an invitation to try and not obvious to accomplish.

In most genetically modified mammalian cells which express heparanase, recombinant heparanase can not be detected in the culture medium, but rather inside the cells. While the '822 patent teaches heparanase secretion in insect cells, secretion of heparanase from mammalian cells was obtained only when the signal peptide of heparanase was replaced by a secretion signal peptide. This replacement is not taught or suggested by the '822 or '735 patents. See Declaration of Iris Pecker, paragraph 5.

In addition, detecting the heparanase in mammalian cells is difficult because most cell lines have a basal heparanase expression. At the time of the subject invention it would have been hard to distinguish the two forms of expression by the ECM assay used by those skilled in the art at the time. Knowing this, the skilled artisan would not have been motivated to try. See Declaration of Iris Pecker, paragraph 6.

In summary, there is no basis to allege that external adhesion of heparanase to cells is inherent. Moreover, successfully expressing mammalian heparanase taught in the '822 patent in the mammalian cell line taught in the '735 patent so as to have "cells in suspension and a purified mammalian heparanase enzyme being externally adhered to said cells, thereby increasing the natural amount of heparanase externally adhered to said cells," as required by the claims, would not have been obvious because a secretion signal peptide is needed. In addition, there is no motivation to produce the recombinant protein unless and until one would be able to distinguish such protein from basal expression.

For these reasons, Applicant respectfully requests that this rejection be withdrawn.

III. CONCLUSION

All of the issues raised in the final Office Action have been addressed and are believed to have been overcome. Accordingly, it is respectfully submitted that all the claims under examination in the subject application are allowable. Therefore, Applicant respectfully requests a Notice of Allowance to this effect.

Respectfully submitted,

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Date: July 28, 2006

Encl:
Request for One-month Extension of Time
Request for Continued Examination (RCE)
Executed Declaration by Dr. Iris Pecker